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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,164	04/09/1999	MICHAEL D. DAN	316082000121	2875

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EXAMINER	
YAEN, CHRISTOPHER H	

ART UNIT	PAPER NUMBER
1642	33

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/194,164	DAN ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,39-50 and 86-133* is/are pending in the application.

4a) Of the above claim(s) *1-25,39-50,119 and 120* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86-118 and 121-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group IV in Paper No. 32 is acknowledged. Claims 88,89, and 133 are canceled without prejudice or disclaimer.

2. Claims 1-25,39-50, and 86-133 are pending, claims 1-25, 39-50, and 119-120 are withdrawn from further consideration as being drawn to a non-elected invention. Applicant is reminded to cancel claims drawn to non-elected inventions.

3. Therefore, claims 86-118 and 121-132 are examined on the merits.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

4. The rejection under 35 USC 112, 1st paragraph as lacking proper written description is maintained for the reasons of record. Although claims 51-85 are canceled, this rejection can be applied to newly added claims 86-118 and 121-132. Applicant argues that the identity of the antigen is not required for the identification of a antigen binding fragment that specifically inhibits the binding of a ScFv or antibody, wherein the ScFv or antibody comprises SEQ ID No: 13. Applicant's arguments have been carefully considered but are not found persuasive. In order for one of skill in the art to adequately practice the instant invention commensurate in scope to the claims, one needs to be able to test whether they were in possession of the claimed polynucleotide. Without the identity of the said "epitope" that is claimed, one cannot adequately determine whether such polynucleotides encoding an antigen binding fragment which specifically inhibits the binding of the said ScFv or antibody comprising

SEQ ID No: 13 was in the possession of the applicant at the time of filing. The specification discloses the use of H11 antibody that binds to the C-antigen. No data beyond the name of the antigen and its presence on cancerous cells has been provided. The extent and nature of the C-antigen is required for the artisan to determine whether polynucleotides that encode antigen binding peptides are available. Because there is a lack of information concerning "epitope" needed for antigen binding peptide in the specification, and because there is no actual reduction to practice of any nucleotide sequence which encodes such antigen binding peptides, the applicant has not demonstrated that they were in possession of the claimed invention at the time of filing.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 90-110, 129, and 131 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:13 and therefore the written description is not commensurate in scope with the claims which read on polynucleotides that encode consecutive amino aicds, consecutive nucleotides, nucleic acid sequences that hybridize under stringent of SEQ ID No: 13, and substitutions, additions or subtractions of the ScFV or antibody of SEQ ID No: 13.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

What are allelic variants? Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined, nor in this case, is the structure of allelic variant proteins encoded by allelic variant genes defined. With the exception of SEQ ID NO:13, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and or encoded variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc.*

V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

No disclosure is made in the specification of the antigen binding peptides or for that matter the nucleotide sequences which encode them. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only the ScFv or antibody comprising the sequence f SEQ ID No: 13 meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112, 1st paragraph

6. Claims 86-118 and 121-132 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a ScFv or antibody comprising the sequence of SEQ ID No: 13 which binds to gliomas, melanomas, and adecarcinomas, does not reasonably provide enablement for a polynucleotide sequence which encodes an antigen binding peptide that specifically inhibts the binding of an ScFv or antibody comprising SEQ ID No: 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn a polynucleotide sequence that encodes an antigen bindinpeptide that specifically inhibits the binding of a ScFv or antibody comprising SEQ ID No: 13 to a cancer cell surface epitope.

The art of record teaches that the extent and nature of the antigen which is being targeted must be understood. Westwood *et al* (Epitope Mapping 2001;chapter 1 pages 5-6) teach that the structure of the antigen (i.e. its folding patern) and the chemical characteristics of the target epitope must be understood for the best immunogeneic response. Furthemore, although antibody-based therapeutics have shown some promising efficacy in the therapy of cancer, (Weiner L.M., Seminars Oncology, Vol. 26, No. 4, Suppl 12, pages 41-50, 1999) one of the obstacles to successful monoclonal antibody therapy is insufficient target specificity. Thus, for an antibody to be somewhat successful there must be a target. In the case of the instant invention, the target is the C antigen expressed on gliomas, melanomas, and adenocarcinomas, and the

specification fails to teach the exact nature of the said antigen. Furthermore, Gura (Science, v278, 1997, pp.1041-1042) discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Therefore, it is well established that cancer in general is a rather unpredicatable disease due to the lack of proper working models.

The specification details the immunological reactivity of the H11 antibody in several cancer types, such as gliomas, melanomas, and adenocarcinomas with normal controls. The specification teaches that this H11 antibody is indeed reactive to primarily cancerous tissues. However, the specification lacks any disclosure concerning polynucleotides that encode antigen binding peptides capable of inhibiting the specific binding of H11 or peptide sequences comprising SEQ ID No: 13. Because cancer types are diverse in etiology and treatment options, there is no correlation made between the cancers disclosed to any and all cancers claimed. This lack of disclosure does not enable the skilled artisan to determine or correlate based on the information disclosed to practice or use the invention on the broad scope of any and all cancers claimed.

Therefore, given the lack of disclosure concerning the antigen, the unpredictability of the cancer field in general, and the lack of information concerning the

unpredicatable nature of the art, one of skill in the art would not be able to practice the invention commensurate in scope to the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Christopher Yaen
Art Unit 1642
September 23, 2003